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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/617,178	07/17/00	EFSTATHIOU S	5673-55696

HM12/1009
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EXAMINER	
ROARK, J	
ART UNIT	**PAPER NUMBER**
1644	14

DATE MAILED: 10/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/617,178	Applicant(s) EFSTATHIOU ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/19/01, 9/26/01 and 10/2/01* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-20 and 22-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-20 and 22-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. The Art Unit location and the examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Jessica Roark, Art Unit 1644, Technology 1600.

2. Applicant's amendments, filed 7/19/01, 9/26/01, and 10/2/01 (Paper Nos. 8, 10 and 12), are acknowledged.
Claim 21 has been cancelled. Claims 1-16 have been cancelled previously.
Claim 28 has been added.
Claims 17 and 20 have been amended.
Claims 17-20 and 22-28 are pending.

3. Sequence compliance: Applicant's provision of a corrected CRF, Sequence Listing, and Statement that the contents are identical on 10/2/01 (Paper No. 12), is acknowledged. The CRF has been found acceptable and entered. However, Applicant is required to identify the sequences with SEQ. ID NOS wherever sequences occur in the specification, drawings, and claims, in order to full satisfy the requirements of 37 CFR 1.821 (d) (see also MPEP 2422.02-2422.03).

In particular, SEQ ID NOS should be provided for the sequences found at least on page 13 of the specification. Applicant is requested to carefully review the specification to determine if additional SEQ ID NO identifiers are required.

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Foreign priority document GB9916703, filed 8/24/01, appears to provide adequate written support for the instant claims 17-20 and 22-27. However, the Examiner was unable to identify support in GB9916703 for an M3 protein that is a coupled protein (claim 28).

5. Applicant's IDS, filed 8/24/01, Paper No. 9, is acknowledged.

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

7. Formal drawings have been submitted which fail to comply with 37 CFR 1.84.
Please see the enclosed form PTO-948.

8. Applicant's amendment of the specification to provide a Section for the "Brief Description of the Drawings" is acknowledged. However, it is noted that drawing descriptions are provided informally on pages 7-8 of the specification. In order to avoid confusion, it is requested that Applicant cancel the description of the drawings found on pages 7-8.

9. Claim 20 is objected to for the following informalities: "fractaline" should be -- fractalkine --, as supported on page 10 of the specification at line 19.

10. Claims 24-26 and 28 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form.

It is noted that in each of claims 24-26 and 28, the addition of a label or a coupled protein broadens, rather than limits the subject matter of claim 17.

In addition, it is noted that the addition of a label appears to be drawn to *in vitro* uses, whereas a coupled protein appears to be drawn to *in vivo* uses. Applicant is invited to consider providing claims that are structured to indicate this.

11. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action. This Office Action will be in response to applicant's arguments, filed 7/19/01 (Paper No. 8). The rejections of record can be found in the previous Office Action (Paper No. 6).

It is noted that New Grounds of Rejection are set forth herein.

12. The cancellation of claim 21 has obviated the previous rejections/objections with respect to this claim.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Applicant's amendment, filed 7/19/01, has obviated the previous rejection of claim 20 under 35 USC 112, second paragraph, as being indefinite in reciting "RNATES".

15. Applicant's arguments, filed 7/19/01 have been found convincing to the extent that the specification does appear to establish the metes and bounds of the phrase "functional homologues". Therefore, the previous rejection of claims 17-20 and 22-27 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn.

16. Claims 17-20 and 22-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17-20 and 22-28 are indefinite and ambiguous in the recitation of "M3" rather than "M3 protein of MHV68" because "M3" represents a laboratory designation that, in the absence of an indication of the virus from which it is derived, is ambiguous and can indicate a number of entities. Applicant should amend the claims to recite the viral origin to unambiguously identify the "M3 protein".

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 17-20 and 22-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method comprising contacting cells with the M3 protein of MHV68, does not reasonably provide enablement for the full breadth of an "M3 protein or functional homologue thereof". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. A person of skill in the art is not enabled to make and use *any* "M3 protein or functional homologue thereof" as encompassed by the full breadth of the claim as currently recited. There is insufficient guidance in the specification to direct a person of skill in the art in how to make and use *any* "M3 protein or functional homologue thereof", other than the M3 protein of MHV68.

After a review of the specification with respect to the nature of an "M3 protein or functional homologue thereof", the specification was not found to provide sufficient guidance to the skilled artisan as to how to make and use an "M3 protein or functional homologue thereof" commensurate in scope with the instant claims. In particular, it is noted that the specification in the bridging paragraph of pages 1 and 2 discloses that "M3 protein or functional homologue thereof" encompasses *any* protein that has at least about 20% homology over the over the whole sequence as compared to the M3 protein of MHV68 and which is capable of binding a chemokine and blocking the binding of the chemokine to its receptor. Further, the specification on page 5 at lines 1-3 indicates that "M3 protein or functional homologue thereof" encompasses derivatives having sequences modified by deletion or substitution.

Although Applicant provides data showing that the M3 protein of MHV68 can bind to several chemokines, the specification does not appear to have established a structural basis for this function. Further, the state of the art did not recognize the structural attributes of the M3 protein needed to bind a chemokine and inhibit binding of the chemokine to its receptor. van Berkel et al. (J. Virol. 2000; 74: 6741-6747) teach that *despite functional similarities* between the M3 protein of MHV68 (also known as γHV68) and the poxvirus CBP-II family, *there is no significant amino acid sequence homology* between M3 and poxvirus CBP-II proteins (see entire document, especially page 6746 2nd and 3rd full paragraphs). van Berkel et al. further teach that the chemokine binding function of various viral proteins likely arose by convergent evolution, because proteins with this function are apparently *unrelated at the primary amino acid sequence level* (see especially page 6746, 3rd paragraph).

Given the breadth encompassed by the instant claims and the absence of a clear structural basis for the recited chemokine binding function; Applicant has not provided the skilled artisan with sufficient guidance as to the identity of residues to be changed, to be left unchanged, or to be deleted. Without clear direction and guidance as to the nature of the changes to be made to the reference M3 protein of MHV68; the skilled artisan would be faced with undue experimentation to produce the immense number of proteins encompassed by a "functional homologue thereof" and determine if there were any operative embodiments that would result in the recited functional activity of binding a chemokine and blocking the binding of the chemokine to its receptor. Thus the specification does not appear to provide the skilled artisan with sufficient guidance to make and use a "functional homologue thereof", commensurate in scope with the claimed invention.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The changes which can be made in the structure of the M3 protein of MHV68 and still provide or maintain the activity of binding a chemokine is unpredictable. Without sufficient guidance, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

19. Claims 17-20 and 22-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of blocking binding of the chemokines lymphotactin, RANTES, MIP-1-(alpha), MCP-1, MCP-4, IL-8, hIP-10, fractalkine, and SLC; does not reasonably provide enablement for the full breadth of the phrase "a chemokine". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. A person of skill in the art is not enabled to make and use *any* "chemokine" as encompassed by the full breadth of the claim as currently recited. There is insufficient guidance in the specification to direct a person of skill in the art in how to make and use *any* "chemokine", other than the chemokines lymphotactin, RANTES, MIP-1-(alpha), MCP-1, MCP-4, IL-8, hIP-10, fractalkine, and SLC.

The specification asserts on page 2 at lines 19-23 that the M3 protein of MHV68 can be used to inhibit the binding of lymphotactin, RANTES, MIP-1-alpha, MCP-1, MCP-4, IL-8, murine KC, murine MIP2, murine LIX, human GCP2, human IP-10 and fractalkine. The specification on page 9 at lines 12-20 discloses that binding complexes are formed between the M3 protein of MHV68 and the chemokines RANTES, MIP-1, and fractalkine. The specification further asserts on pages 9-10 that data disclosed in Figure 2 as well as data not shown supports that the binding of the M3 protein of MHV68 to RANTES, MIP-1, or IL-8 can be competed to some extent "by all unlabelled chemokine competitors tested". Figure 2 is disclosed as including competition data for hRANTES, mRANTES, hMIP-1, mMIP-1, vMIP-II, MCP-1, MCP-4, mKC, hGRO, hIL-8, mMIP-2, mLIX, hGCP-2, IP-10, lymphotactin, and fractalkine.

It is noted that the quality of the instantly provided figures is too poor to permit firm conclusions to be drawn; however, Figure 2 raises the question of whether the data support Applicant's assertions with respect to the chemokines murine KC, murine MIP-2, and murine LIX.

It is further noted that Parry et al. (J. Exp. Med. 2000; 191:573-578, of record) show in Figure 3 competition data with increasing concentrations of competitor chemokines versus labeled IL-8 and MIP-1-alpha; but not show inhibition with the chemokines murine KC, murine MIP-2 and murine LIX (as well as human BCA-1 and human SDF-1-alpha), even in the presence of a 2000 molar excess of competitor (Figure 3 on page 576). Similarly, van Berkel et al. (J. Virol. 2000; 74: 6741-6747) teach that while several chemokines appear to interact with the M3 protein of MHV68 (also known as γHV68); murine CXC chemokines (including mKC, mMIP-2 and several others), do not appear to do so (see especially Figure 2 on page 6743, and Table 1). Given the large number of human and murine chemokines that are known (plus those as yet undiscovered); the data disclosed in the specification does not appear to reasonably predict to which chemokines the M3 protein of MHV68 will bind and inhibit binding of that chemokine to its receptor. This is particularly true with respect to the murine chemokines of the CXC class, as noted by van Berkel et al. supra.

Given that the instant claims encompass (claims 17-19 and 22-28) and recite (claim 22) non-enabled embodiments; the specification does not appear to provide the skilled artisan with guidance commensurate in scope with the claimed invention. Therefore, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

20. Applicant's provision of the certified copy of Great Britain Application No. GB9916703, filed 8/24/01, and establishing that Parry et al. (of record) is not available as prior art under 35 USC 102(a); has obviated the previous rejection of claims 17-27 under 35 USC 102(a) as being anticipated by Parry et al.

21. No claim is allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
October 9, 2001

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
10/9/01

Attachment for PTO-948 (Rev. 03/01, or earlier)
6/18/01

The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.